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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,420	MARDH, SVEN	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-16* is/are pending in the application.

4a) Of the above claim(s) *14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority und r 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachm nt(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment filed 9-22-03 has been entered. Claims 1, 2, 8, 10, 11 and 13 have been amended. Claim 3 has been canceled. Claims 1, 2 and 4-16 are pending and claims 1, 2 and 4-13 are under consideration.

Priority

1. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), **the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications**. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application. No relationship between Application No. 09/603,153 and 09/09/117,798 has been disclosed. Appropriate correction is required.

Specification

The amendment filed 9-22-03 amending the specification by inserting before the first line "This application is a continuation...Swedish Application No. 9600434-6, filed February 6, 1996,

the contents of each of which application is herein specifically incorporated by reference in its entirety" is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The oath/declaration of the present application is the original oath/declaration of parent application 09/117,798 but fails to incorporate herein by reference its parent applications. Thus, the amendment filed 9-22-03 introduces new matter into the specification.

Terminal Disclaimer

2. The terminal disclaimer filed on 9-22-03 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of patent No. 6,497,874 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Objections

3. Claims 4-10 are objected to because of the following informalities: Claims 4-10 depend on claim 1, therefore, the term "A" in each claim should be changed to "The". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 2 recites the limitation "The method of claim 1" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 1 is a product claim not a method claim. Applicant's amendment filed 9-22-03 necessitates this new ground of rejection.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2 and 4-13 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing a bacteriophage B8 expressing ScFv-M13 gene 3 fusion protein, wherein ScFv is single-chain Fv containing V_H and V_L chains of antibody against H. pylori antigen and gene 3 is a surface protein of M13 bacteriophage, and shows reduction of H. pylori cell number when infected with said bacteriophage B8 *in vitro*, does not reasonably provide enablement for any modified bacteriophage for use in the treatment or prophylaxis of any type of bacterial infection, such as a Helicobacter pylori infection, *in vivo* via various administration routes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 4-18-03 (Paper No. 7). Applicant's arguments filed 9-22-03 have been fully considered but they are not persuasive.

Applicant argues that the claims have been amended to read on treatment of prophylaxsis of a Helicobacter pylori infection and the specification teaches how to make and use the claimed

bacteriophage and means of administration of the modified bacteriophage (amendment, p. 8-9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 4-18-03 (Paper No. 7). Although the method of making and administering the claimed bacteriophage were known at the time of the invention, the use of phage as a therapy for infectious bacterial diseases was inconsistent and unpredictable in its results because the great potential of these viruses to kill bacteria *in vitro* was not realized *in vivo*. Further, administration route of the modified bacteriophage can affect the amount of the modified bacteriophage to reach target cells so as to provide therapeutic effect *in vivo* and to ameliorate the bacterial infection. Therefore, one of skilled in the art at the time of the invention would not know how to administer the claimed bacteriophage to a mammal via various administration routes such that said administration could provide therapeutic effect for the treatment or prophylaxis of a Helicobacter pylori infection *in vivo*. Thus, one skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 2, 4-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winter et al., 1994 (Annual review of Immunology, Vol. 12, pp. 433-455). Applicant's amendment filed 9-22-03 necessitates this new ground of rejection.

Claims 1, 2, 4-9 and 12 are directed to a modified bacteriophage such as M13 bacteriophage, for the treatment or prophylaxis of a bacterial infection, such as a Helicobacter pylori infection *in vitro* and *in vivo*, and the bacteriophage presents at its surface a recombinant protein containing a bacteriophage surface protein, such as gene 3 protein, and a variable region of an antibody, such as ScFv polypeptide, to provide a bacterial antigen binding site, and a pharmaceutical composition containing said bacteriophage and a pharmaceutically acceptable carrier or excipient.

Winter teaches construction of phagemids expressing fusion proteins containing various antibody V fragments and filamentous bacteriophage gene III protein (pIII), and production of recombinant phages particles via rescue with a helper phage M13K07, wherein the fusion proteins containing antibody fragments and pIII are displayed on the surface of the recombinant phages. The phages are selected by binding to antigen, and soluble antibody fragments are secreted from infected E. coli bacteria. The antibody includes antibody against carbohydrates, cell-surface protein, and viral coat protein etc., (e.g., abstract, introduction, p. 435, 436). The buffer solution containing the recombinant phages is considered a pharmaceutical acceptable carrier.

Although Winter does not specifically teach using a variable region sequence of an antibody against Helicobacter pylori, however, Winter does teach construction of phagemids expressing fusion proteins containing various antibody V fragments and filamentous bacteriophage gene III protein, and the antibody includes antibody against carbohydrates, cell-surface protein, and viral coat protein etc. Thus, it would have been obvious for one of ordinary skill in the art at the time of the invention to use V fragments of antibody against Helicobacter

pylori for the construction of the modified bacteriophage because antibody against Helicobacter pylori could be an antibody against cell-surface protein or carbohydrates. One of ordinary skill at the time the invention was made would have been motivated to do so in order to produce recombinant phages particles and the secretion of soluble antibody fragments from infected E. coli bacteria as taught by Winter with reasonable expectation of success.

It should be noted that the intended use of the claimed modified bacteriophage does not carry weight in 35 U.S.C. 103(a) rejection.

Conclusion

No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.